Remarks/Arguments

Claims 1-11, 14, and 19-24 are pending in this application. Claim 14 has been amended; support for the amendment to claim 14 can be found in claim 1. No new matter has been added by this amendment. Claims 12, 13, and 15-18 have been canceled. Claims 19-22 have been withdrawn.

Claim 14 remains rejected under 35 U.S.C. §102(b) as anticipated by Arnolds-Stanton et al., J. Org. Chem. 56(1):151-157 (1991). The Examiner asserts that Arnolds-Stanton et al. disclose compound 13 obtained in a mixture with other compounds. The Examiner is of the opinion that this mixture constitutes a pharmaceutical composition according to the claims. Applicants do not agree with the Examiner's assertions for the reasons set forth in their previous Amendment, but for purposes of advancing prosecution they have amended claim 14 to include the proviso from claim 1. As the Examiner has admitted that Arnolds-Stanton et al. does not anticipate the compounds claimed in claim 1 because they are excluded from the scope of the claims by the proviso, it follows that Arnolds-Stanton cannot anticipate the pharmaceutical compositions claimed in claim 14.

Claims 1-11, 14, and 23-24 remain rejected under 35 U.S.C. §103(a) as obvious over Mu et al., Colloids and Surfaces A: Physiochem. Eng. Aspects 181:303-313 (2001). The Examiner asserts that Mu et al. disclose ethyl 2,4-dihydroxybenzoates with fluoroalkyl substituents, that the difference between the compounds disclosed in Mu et al. and the claimed compounds is simply the

length of the fluoroalkyl substituent R_3, and that the compounds are prima facie obvious over the compounds disclosed in Mu et al. The Examiner also states that Applicants claim compounds with an alkyl group at position R_1, while Mu et al. disclose compounds with a hydrogen substituent at R_1 instead of an alkyl substituent. Applicants traverse.

Scheme 1 in Mu et al. shows a synthesis scheme for a methyl siloxane polymer incorporating side groups. According to Scheme I, the compounds are prepared by introduction of a fluorocarbon chain at position four of ethyl 2,4-dihydroxybenzoate using a Mitsunobu reaction. The compound obtained from this step, ethyl 4-(2-perfluorooctylethoxy)-2-hydroxybenzoate (hereinafter referred to as "compound A"), is the most similar of any of the compounds disclosed by Mu et al. in scheme 1 to the compounds claimed in claim 1 and claim 23. Mu et al. also disclose ethyl 4-(2-perfluorohexylethoxy)-2-hydroxybenzoate ("compound B") and ethyl 4-(2-perfluorobutylethoxy)-2-hydroxybenzoate ("compound C"). However, none of these are a compound of the claimed invention because the fluroalkyl chain is ten, eight, and six carbons long, respectively, whereas the present application claims compounds with fluorocarbon chains between one and five carbons in length. Furthermore, Mu et al. disclose no useful properties of compounds A, B, or C. In fact, Mu et al. only use these as intermediates in the synthesis of other compounds.

Immediately after synthesizing compound A, the authors teach introducing an alkene group at the 2 position of the benzene ring by adding 3-bromopropene. The product of this reaction is not a compound of the present invention because

the present invention claims compounds where R_2 is hydrogen or an acyl substituent. The following step in the Mu et al. synthesis is deprotection of the ester group in basic media to obtain the corresponding acid. After that step, the acid is combined with 4-cyanophenyl 4-hydroxybenzoate to generate a monomer which is then combined with a methyl siloxane polymer to generate the polymers P1, P2, and P3. The polymers P1, P2, and P3 are the subject of the discussion in the Mu et al. article, and Mu et al. do not discuss any physical, chemical, or pharmaceutical properties of compounds A, B, or C. One having ordinary skill in the art would recognize that compounds A, B, and C are merely intermediates in the synthesis of the monomer, which is itself an intermediate in the synthesis of the polymers P1, P2, and P3.

From the foregoing discussion, it is clear that it would not have been obvious to one of ordinary skill in the art to modify compounds A, B, or C to arrive at the compounds of claims 1, 10, 11, or 23-24, or at the pharmaceutical compositions of claim 14 because one having ordinary skill in the art would not have any motivation to modify compounds A, B, or C. The Examiner argues that the Supreme Court's decision in KSR v. Teleflex Inc., 127 S.Ct. 1727 (2007) forecloses the argument that there exists no motivation in the art to modify the prior art compounds. KSR v. Teleflex held that an invention may be obvious when there is a design need or market pressure to solve a problem and there are a finite number of identifiable, predictable solutions, and that it is not necessary to show some teaching, suggestion, or motivation in the art to use one of those solutions to show obviousness. Id. at 1742. However, the Federal Circuit has

held that, even in light of KSR, in cases involving claims directed to new chemical compounds, "it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound." Takeda Chemical Industries v. Alphapharm PTY, 492 F.3d 1350, 1356-7 (Fed. Cir. 2007). Hence, it still remains necessary to show both a reason why one of skill in the art would select compound A, B, or C as a starting point for investigation, and a reason why one of skill in the art would shorten the fluoroalkyl chain of compound A, B, or C to arrive at the compounds of claims 1-11, 23, and 24, and the pharmaceutical compositions of claim 14, in order to show that these claims are prima facie obvious over the prior art.

Applicants respectfully submit that neither showing has been made in this case. First, there is no motivation to select one of compounds A, B, or C as a starting point for investigation. The Federal Circuit has held that if the prior art only discloses compounds as intermediates in the production of a final product, one of ordinary skill in the art would not be motivated to stop the reference synthesis and investigate the intermediate compounds with an expectation of arriving at a useful compound. See In re Lalu, 747 F.2d 703, 707 (Fed. Cir. 1984); see also Manual of Patent Examining Procedure §2144.09.VI (8th Ed. R. 7, 2008). Here, Mu et al. only disclose that compounds A, B, and C are useful as intermediates in the synthesis of liquid crystal polymers. Mu et al. do not disclose that the compounds have any useful properties other than as intermediates in the synthesis of liquid crystal polymers. No motivation exists in the art to stop the

synthesis of the liquid crystal polymers in Mu et al. and investigate the intermediate compounds.

Second, even assuming *arguendo* that some motivation exists to modify compounds A, B, and C disclosed by Mu et al, there exists no motivation to shorten the fluoroalkyl chains of these compounds. In other words, the prior art teaches away from modifying compound A, B, or C to arrive at the compounds of the present invention. The polymers of Mu et al. are said to be useful as liquid crystals. The paper indicates that polymers with longer fluoroalkyl chains work better for several reasons.

First, polymers of the type investigated by Mu et al. that incorporate fluoroalkyl chains tend to exhibit a smectic phase, whereas similar polymers without such chains only exhibit a nematic phase. See page 304, first column. Indeed, Mu et al. disclose a polymer P4 that incorporates a hydrocarbon chain and does not exhibit a smectic phase. Mu et al. further disclose that the polymer P1, which has a short (6C) fluoroalkyl side chain, exhibits a nematic phase transition and no smectic phase transition, similar to P4, which incorporates a non-fluorinated hydrocarbon chain. See page 307, second column. However, the polymers incorporating longer fluorakyl chains, P2 and P3, each exhibit a smectic A phase transition. See page 307, second column. The authors note that "introduction of the perfluorocarbon chain to polymers facilitates the smectic properties." See page 304, first column. The fact that introducing shorter perfluorocarbon chains failed to introduce smectic properties into the polymers

would cause one of skill in the art to lengthen, rather than shorten, the perfluoroalkyl chains.

Second, Mu et al. disclose that prior polymers incorporating shorter fluoroalkyl chains tend to behave similarly to polymers incorporating hydrocarbon side chains. As the authors note in the second column on page 304:

> The monolayer formation and [Langmuir-Blodgett] film deposition of these polymers are improved by varying the hydrophilicity of the backbones and hydrophobicity of the side chains. Fluorocarbon chains are known to be more hydrophobic and rigid than their hydrocarbon analogues. The introduction of the shorter fluorocarbon chain in the side chain leads to a similar effect to the longer hydrocarbon side chain. The monolayer properties of fluorinated polymers depend on the length of the fluorocarbon chain.

As stated above, polymers incorporating hydrocarbon side chains failed to exhibit a smectic phase transition. Furthermore, as noted above, the authors of the paper were looking for a way to introduce smectic properties into the polymers. Considering this, one of ordinary skill in the art would be motivated to lengthen the fluorocarbon chain, whereas in order to obtain the claimed compounds, one of skill in the art would have to shorten the fluorocarbon chain. Therefore, one of ordinary skill would have to go against the teachings of Mu et al. to arrive at the claimed compounds.

Finally, Mu et al. teach that longer fluoroalkyl chains enhance the collapse pressure of the liquid crystals. See the paragraph bridging columns 1 and 2 on page 311. The paper also concludes that the length of the perfluoroalkyl chains affects the stability of the monolayer and the packing of the side chains at the air-water interface and that strong interactions between long fluorocarbon chains are

necessary to stabilize the layer structure in multilayer LB films. See the last paragraph of text on page 312. One reading this paper thus would come away with the conclusion that longer fluoroalkyl chains are desired, and as such the paper teaches away from developing compounds with a fluorinated alkoxy chain of less than 6 carbons.

The teachings of Mu et al. do not render claim 14 obvious for substantially the same reasons stated above. In addition, the teachings of Mu et al. do not render claim 14 obvious because it would not have been obvious from the disclosure in Mu et al. to combine the intermediates of the polymer synthesis with one or more pharmaceutically acceptable excipients. Mu et al. do not disclose that the intermediates of the polymer synthesis have any pharmaceutical activity, nor do they suggest combining the intermediate compounds with a pharmaceutically acceptable excipient. As such, the pharmaceutical compositions of claim 14 would not have been obvious over the compounds disclosed by Mu et al.

Further, the teachings of Mu et al. do not render claims 6, 10, 11, and 24 obvious. Claim 6 covers a compound of claim 1 or 2 wherein R_1 is 2,2,3,3,3-pentafluoropropyl. Claim 10 covers 2-hydroxy-4-(2,2,3,3,3-pentafluoropropoxy)benzoic acid or a salt thereof, and claim 24 covers 2-hydroxy-4-(2,2,3,3,3-pentafluoropropoxy)benzoic acid. Mu et al. teach no compounds wherein the second carbon of the alkoxy substituent at the four position on the benzoate ring is perfluorinated, i.e. substituted with two fluorine atoms. Mu et al. furthermore do not provide any motivation for replacing the

hydrogens on the second carbon in the alkoxy chain with fluorines. Likewise, the compounds claimed in claim 10 and 24 are not obvious over the compounds disclosed by Mu et al. for the same reason. Furthermore, Mu et al. do not render claim 11 obvious. Claim 11 claims 2-acetoxy-4-(2,2,3,3,3-pentafluoropropoxy)benzoic acid or a salt thereof. Mu et al. do not teach any compounds where the second position of the benzene ring is substituted by an acetoxy group and furthermore do not teach modifying the hydroxyl group at position 2 to form an acetoxy group.

Submitted herewith is a translation of the priority application per the Examiner's request.

In view of the foregoing amendments and remarks, Applicants respectfully submit that the claims of the application are in condition for allowance. Applicants request that when the product claims are found to be allowable, the withdrawn process claims be considered for rejoinder, as indicated in the Office Action of June 5, 2007.

The Director is authorized to charge any fees or overpayment to Deposit Account No. 02-2135.

Respectfully submitted,

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